This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

DRAFT VERSION

ELECTRODE RECORDING CATHETER PRELIMINARY GUIDANCE

Data to be Submitted to the Food and Drug Administration
in Support of Premarket Notifications

Mark Massi

Pacing and Electrophysiology Devices Branch
Division of Cardiovascular, Respiratory, and Neurological Devices
Office of Device Evaluation

March 1995

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

CONTENTS

ELECTRODE RECORDING CATHETER PRELIMINARY GUIDANCE

Introduction

An electrode recording catheter is defined in Title 21 of the Code of Federal Regulations (21 CFR 870.1220) as a unipolar or multipolar device that is used to detect an intracardiac electrogram. These catheters may be either fixed curve or deflectable, and may also be used for cardiac stimulation during diagnostic procedures. Only catheters that are from 3 Fr to 8 Fr in diameter with cylindrically-shaped electrodes, which are less than 5.0 mm in length and are of same nominal diameter as the tubing diameter, are within the scope of this guidance. Electrode catheters for detection of cardiac output and left-to-right shunts, and temporary pacemaker electrodes (21 CFR 870.3680) for therapeutic pacing are not within the scope of this document.

If you intend to market catheters with larger electrodes, you must either: 1) provide documentation of pre-Amendments status for an electrode recording catheter with electrodes of greater than 5.0 mm in length that was labeled or promoted for the same diagnostic intended uses, and provide data demonstrating your device is substantially equivalent to that pre-Amendment device; or, 2) obtain clinical data that demonstrates your device is substantially equivalent to a predicate device with less than 5.0 mm electrodes by demonstrating that the different technological characteristics do not raise different questions of safety and effectiveness and that your device is as safe and effective as a predicate device. Any electrode recording catheter with temperature measurement features, or any deflectable catheter which permits infusion through or within the electrodes, are assumed to be intended for catheter ablation and are, therefore, class III, Premarket Approval devices.

This preliminary guidance was developed in order to provide a description of the type of information that the Food and Drug Administration (FDA) anticipates to support substantial equivalence with a legally marketed predicate device. The guidance should supplement the information that is required under sections 510(k), 513(f), and 513(i) of the Federal Food, Drug and Cosmetic Act (Act) and part 807, subpart E of 21 CFR. Questions may be directed to the Pacing and Neurological Devices Group at (301) 443-8517. Questions concerning a temporary pacemaker electrode may be directed to the Interventional Cardiology Devices Group at (301) 443-8243.

Intended Uses

These devices are commonly placed at the high right atrium, right ventricular apex, and His bundle, and in the coronary sinus, and are used for electrogram recording and cardiac stimulation during diagnostic electrophysiology studies. Indications for use include evaluation of sinus node dysfunction, atrioventricular conduction, intraventricular conduction disturbances, tachyarrhythmias, and unexplained syncope or cardiac arrest.

Labeling Requirements

Submit copies of all proposed labels, labeling, and advertisements that are sufficient to describe the device, its intended use, and the directions for use. The labeling must contain an indications for use statement, including recommendations for the use of a particular catheter model for a given clinical situation, contraindications, warnings, and precautions.

The label and directions for use for devices with electrodes that are greater than 2.0 mm in length or which permit infusion through an electrode must include the following statement:

> CAUTION - The safety and effectiveness of this device as an ablation catheter have not been established. Therefore, such use is considered investigational.

The label and directions for use for devices which are less than 1.0 mm in diameter must include the following statement:

> CAUTION - The safety and effectiveness of this device for coronary artery mapping has not been established. Therefore, such use is considered investigational.

Device Description

A complete materials list should be provided. Identify polymers by generic name, manufacturer, trade name and formulation, and include adhesives, coatings, and color or other additives in the list. Color additives are subject to section 721 of the Act and part 71 of 21 CFR unless exempt from certification under part 73 subpart D; confirm the status of the color additives that are used in the design.

Submit dimensional drawings of the catheters with reasonable tolerances, and a detail drawing of the distal portion of the catheter on which you clearly indicate the attachment point of the steering wire(s), and the size and location of the electrodes. Specify the general shape, the nominal radius of curvature, bend angle, and length of the distal section for each model.

Show the layout of the internal construction of the catheter with detail drawings of the main body and distal tube cross-sections. Provide a prose and pictorial description of the steering mechanism, if applicable.

Describe the accessory cables which are intended to be used with the catheters; include dimensional drawings of the cables and detail drawings of the connectors. Patient-connected leads shall comply with Section 12A of Underwriters Laboratories UL 544 Standard for Safety.

Biocompatibility

Submit your complete biocompatibility test protocols, acceptance criteria, results, analysis, and conclusions on all materials which may contact blood or other tissues. State whether standard test procedures were used, or provide justification for not adhering to commonly accepted methods. Describe the sample preparation, including the portions of final, sterilized catheters that are used, and justify your choice for the sample in each test procedure. Elutions should be prepared with both polar and non-polar solvents, where applicable. Use the Tripartite Biocompatibility Guidance for Medical Devices to anticipate the information needed for the evaluation of the toxicity of your catheters.

Electrode recording catheters are defined as short-term duration, direct blood path, externally communicating devices under the guidance, for which the suggested biological tests in Table I have been identified.

Irritation Tests	Acute Systemic Toxicity	Mutagenicity
Sensitization Assay	Material Mediated Pyrogenicity	Subchronic Toxicity
Cytotoxicity	Implantation Tests	Hemocompatibility/ Hemolysis

Table I. Biological Tests

Note that the guidance refers to hemocompatibility, and not just hemolysis. Hemocompatibility studies should be conducted, if the materials which contact blood are new as compared to the legally marketed predicate devices. The International Organization for Standardization Draft International Standard "Biomedical Testing of Medical and Dental Materials and Devices - Part 4" (ISO/DIS 10993-4) is a useful reference for the selection of tests for interactions with blood.

If the manufacturer or importer determines that biocompatibility testing is not necessary for a given submission, and the test reports have been previously submitted, a table of the following information should be provided: the materials which contact blood or other tissue;

the samples used in the tests; the biocompatibility tests for each material; and, references to previous applications which contain those test reports. A discussion of any changes in formulation, manufacturing, or processing, including sterilization, which could affect biocompatibility, and a scientific justification for the omission of additional tests should be provided. We would consider cytotoxicity, hemolysis, and the limulus amebocyte lysate (LAL) tests with finished, sterilized catheters to be minimal biocompatibility tests for any new Premarket Notification.

Sterility

The submitter should describe the sterility test protocol, and state whether routine package verification (seal integrity), and sterility and LAL testing will be performed on samples of each sterilization lot. State the proposed sterility assurance level, and identify the portion of the device which you have determined to be the most difficult to sterilize. If the following sections on ethylene oxide or gamma radiation sterilization do not apply, describe the sterilization process and provide a detailed description of the validation method.

Ethylene Oxide Sterilization

Specify whether the overkill or bioburden method (ANSI/AAMI ST27-1988), or some other method, is used in the validation of the sterility assurance level. If the bioburden method is used, show the correlation of the numbers and resistance of the bioburden to the indicator microorganism; describe the method of microbial resistance determination. Identify the microbial challenge that is used in the validation.

Specify the maximum residual levels for ethylene oxide, ethylene glycol, and ethylene chlorohydrin. The manufacturer should comply with the maximum residual limits for implant devices as published in the Federal Register, volume 43, number 122, pages 27482-3. Completely describe the measurement method that is used to verify that the device controls and aeration meet the requirements for maximum residual levels (ANSI/AAMI ST29-1988 and ST30-1989, for example).

Gamma Radiation Sterilization

Verify the completion of dose mapping, including the identification of minimum and maximum zones and the method of dosimetry (ANSI/AAMI ST32-1991).

Specify the radiation dose and whether the dose setting method is based on a validation method in the ANSI/AAMI guideline. Identify the specific validation method and the microbial challenge used in the validation.

Packaging

Specify the primary packaging materials and adhesives to be used and include a dimensional drawing of the primary package. Verify whether the materials, device configuration, and packaging process for the current device are identical to those which are used for the predicate devices. If the materials, device configuration, and processing are identical, and the predicate device labeling bears an expiration date, then the labeling for the new device must bear the same expiration date. If the packaging materials, device configuration, or processing are not the same, or the device materials raise new concerns about long-term stability, then we believe that you must determine the expiration date.

In order to document your determination of expiration date, and demonstrate the adequacy of the packaging system in protecting the integrity and maintaining the sterility of the contents, you should provide a report on:

real-time or accelerated aging (show calculations); ___

shipping tests with the same samples (preconditioning, vibration, drop, and compression, as described in ASTM D 4169, for example); and,

maintenance of sterility verification and device performance testing.

If the final package design is identical to that of the predicate device and this information may be found in a previous submission, summarize the information and provide a reference to that file.

Provide shipping and storage recommendations in the labeling,

If a portion of the device is intended for resterilization and re-use, you should provide information on the functional testing which you conduct and which demonstrates the acceptability of the device after the maximum number of permitted sterilization cycles. Because accessory cables are typically sterilized and re-used, specify in the labeling: the recommended sterilization method; the minimum aeration time if ethylene oxide is the sterilant (show dissipation curves for ambient conditions); and, either a maximum number of re-uses or a routine validation test method.

Performance Testing

The design validation test reports must include the test protocol, pass/fail criteria, results, analysis of the results, and conclusions. The pass/fail criteria should be based on the minimum device specifications which were developed prior to the design validation testing and which you can justify in light of the intended use of the device. Present the results as the range of values, mean and standard deviation, or 95% confidence interval, where it is applicable. A probability measure, that is indicative of the statistical significance of the any comparisons, should be provided. This testing should be performed with an adequate number of catheters or subassemblies with the minimum and maximum length, diameter, number of conductors, et cetera, which may affect the outcome of the test; justify the number of samples used in each test. If only one version was used in a particular test, discuss your rationale for not using other versions. All testing must be conducted on sterilized, fully processed catheters or subassemblies.

Reliability Testing

Verify electrical continuity and isolation, and mechanical integrity of sterilized catheters or subassemblies after thermal cycling (MIL-STD-202F, Method 107G, Test Condition A with 30 minute dwells, for example).

A. Determine the strength of each bond in the catheter (lower 95% confidence bound). Document the mode of failure in each of the pull tests. Tensile testing should include the following:

   1. Tip electrode/tubing subassembly;
   2. Tubing joint subassembly;
   3. Cable/handle; and,
   4. Cable/connector.

   The subassemblies (items 1 and 2) should not include the conductors, steering wires, safety wires, et cetera; these tests are intended for validation of the bond for the identified components only.

B. Determine the torque and twist angle to failure (lower 95% confidence bound) for tubing joint subassemblies as described in item A(2) above. For consistency, it is recommended that the joint be centered in the test fixture such that approximately 5 cm of the sample are free to rotate. Document the mode of failure in each trial. This test is not applicable for catheters constructed from a single, continuous tube.

C. Determine the torque and twist angle of the handle with respect to a fixed tip electrode, that result in a failure of the catheter (lower 95% confidence bound). Document the mode of failure in each trial. Report the results for both directions of angular rotation and at least the shortest catheters with the largest diameter (i.e., maximum radius-to-length ratio).

D. Further document the integrity of the tip/tubing and distal catheter joints by recording the gas pressure that results in leakage; document the location of the leak in each trial.

Subassemblies may be used. Alternatively, you may show that the internal components of the catheter are sterile and biocompatible.

E. Determine the catheter leakage current after soaking in a saline solution for duration of time consistent with the intended use of the device, such as 8 hours. At least the smallest diameter catheters with the largest number of conductors should be tested. Record the largest current when a voltage (100 VDC, for example) is applied between the conductors and an external bath, and while the catheter is submersed in the conductive solution.

F. Subject the catheter steering mechanism to a number of deflection cycles, which is representative of the number of deflections in a typical study plus a safety factor (100 cycles, for example). A deflection cycle is actuation of the steering mechanism through an entire range of motion. Confirm electrical continuity and isolation, and catheter integrity at the end of the test.

G. Subject the catheter/handle joint to a number of flexion cycles. Confirm electrical continuity and isolation, and catheter integrity at the end of the test.

Determine the engagement and separation forces for each connector type.

Subject the accessory cables to pull tests (cable/connector joint) and flex fatigue in order to demonstrate the durability of the cables for repeated use. Also determine the dielectric strength of the accessory cables (Standard for ECG Connectors (AAMI ECGC), for example). If this information may be found in previous premarket notifications, summarize the information and provide references to those file numbers.

Samples of each dimensionally different open lumen catheter should be subjected to the following tests, if applicable:

A. Determine typical stylet insertion and withdrawal forces.

B. Plot typical pressure versus infusion rate curves.

C. Determine the pressures (lower 95% confidence bound) that result in catheter leaks or other loss of integrity. The catheter labeling should state maximum pressures and corresponding flow rates that are less than one-half the lower bound.

D. Determine the natural frequency and damping coefficient to demonstrate the performance of the device for invasive blood pressure measurements. Alternatively, you may determine the magnitude response of the catheter and show that the phase response is linear over the physiologic bandwidth.

Materials and Mechanical Performance

Since some polymers may soften at body temperature, the following tests should be performed under simulated use conditions. Such conditions may involve submersion of the catheter in a saline bath at 37° Celsius for a duration that is consistent with the intended use (8 hours, for example). The catheter may also be passed through a U-shaped tube to simulate the aortic arch or other severe bend. Discuss your choice of the vascular model, and the effects of the model dimensions on the test.

A. Describe the effect of twist angle and tubing diameter on applied torque. This testing should be performed with the catheter main body tubing and internal structural elements at 37° Celsius, but not with the short, flexible, distal tubing in deflectable catheters. Generate a plot of the results (Γ versus ϕ / ℓ), and approximate the product of shearing modulus of elasticity and moment of inertia by: $\Gamma = (G \cdot J)\ \phi / \ell$, where Γ is the torque, ℓ is the length of the sample, and ϕ is the angle of twist.

B. Submit statistics on applied force of the distal tip from the 90° position (1) during full actuation of the deflection mechanism without translation, and (2) as a result of translation (i.e., pull-back) of the catheter without further deflection, for the various curve configurations. Determine the applied force in an orthogonal plane for catheters with "orthogonal steering" or "lateral deflection" features, and provide a discussion and justification for your choice of catheter constrainment.

C. Provide a discussion for simulated steering of the finished catheter—advancement withdrawal, and rotation—through a vascular model.

Using the same catheters and subassemblies from the torque and steering tests above, perform the following stiffness tests at room temperature to assess worst-case properties. Discuss upper limits on bending resistance both along the catheter main body and at the distal tip which may result in damage to vascular or cardiac structures. Compare worst case stiffness with the predicate device; significant increases in stiffness may require clinical study to assess the impact of the device differences on safety and effectiveness.

A. Describe the effect of applied weight and diameter on tubing deflection. This testing should be performed with the catheter main body tubing and internal structural elements, but not with the short, flexible, distal tubing in deflectable catheters. Fix both ends of the sample and apply the weight at the midpoint. Generate a plot of the results (f versus $W \cdot \ell^3$) and approximate the product of modulus of elasticity and moment of inertia by: $f = (1/192(E \cdot I))\ W \cdot \ell^3$, where f is the deflection, ℓ is the length of the sample, and W is the weight.

B. Design a test to measure the force required to cause a finished, undeflected catheter to buckle. Justify your choice for the length of unconstrained catheter, and use at least large-diameter, closely-spaced multipolar catheters with short distal tubes in the testing.

Determine the radiopacity of the compounded tubing by the ASTM F 640 Standard Test Methods for Radiopacity of Plastics for Medical Use. Method C is recommended for consistency among manufacturers; show all calculations.

Electrical Performance

Determine the direct current resistance and impedance at 5,000 Hz of each conductor for all possible combinations of catheters and accessory cables. Connect unused leads to reference ground during the impedance test. If magnitude of the impedance differs significantly from direct current resistance, determine the magnitude of the reactive component of the impedance, and explain why the measured values do not affect stimulation or recording performance, or limit the use of the catheters with currently marketed stimulators or recording devices.

Describe the features which are implemented in the design to reduce the susceptibility of the catheters and cables to noise. Quantify typical peak and average noise levels for the various combinations of catheter and accessory cable (for example, the signal-to-noise ratio for the largest His bundle electrogram).

If the electrode design or configuration are different than the predicate device, investigate the stimulation thresholds for the device (high right atrium and right ventricular apex gain-of-capture thresholds). Compare the results to those obtained with the predicate devices.

If your device differs from the standard electrode recording catheter design, as described in the Introduction section above, you may be required to provide clinical data to verify the performance of the device for mapping. You must assess the effects of electrode size and distribution on the accuracy and reliability of the information obtained with the device. Develop adequate labeling to describe the use of the device in guiding therapy, and the limitations of the device for mapping. Clinical data will also be required to support substantial equivalence of electrode catheters that are less than 1.0 mm in diameter, since they may be used in the coronary vasculature or for special applications. Prospective studies are considered significant risk for which you must obtain Investigational Device Exemptions (IDE) approval from FDA. Given that diagnostic studies may lead to a therapeutic procedure, such procedures must be performed with legally marketed therapeutic devices used in accordance with the labeling, or with investigational devices that are part of the same study.

Quality Assurance

Outline the quality assurance tests and release criteria, which you will use during production of the catheters.

Truthful and Accurate Statement

Under 21 CFR 807.87(j), the person required to submit the premarket notification must state that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

510(k) Summary or Statement

Under 21 CFR 807, the person required to submit the premarket notification must submit either (1) a summary of the safety and effectiveness information in the premarket notification submission upon which an equivalence determination could be based (510(k) Summary, 21 CFR 807.92), or (2) a statement that safety and effectiveness information will be made available to interested persons upon request (510(k) Statement, 21 CFR 807.93).

Referenced Documents

Federal Food, Drug, and Cosmetic Act

Code of Federal Regulations, Title 21 - Food and Drugs

Tripartite Biocompatibility Guidance for Medical Devices

International Standards Organization Draft International Standard, Biomedical Testing of Medical and Dental Materials and Devices (ISO/DIS 10993)

Underwriters Laboratories Standard for Safety (UL 544)

Association for the Advancement of Medical Instrumentation:

> Guideline for Industrial Ethylene Oxide Sterilization of Medical Devices (ANSI/AAMI ST27-1988)
>
> Recommended Practice for Determining Residual Ethylene Oxide in Medical Devices (ANSI/AAMI ST29-1988)
>
> Determining Residual Ethylene Chlorohydrin and Ethylene Glycol in Medical Devices (ANSI/AAMI ST30-1989)
>
> Guideline for Gamma Radiation Sterilization (ANSI/AAMI ST32-1991)
>
> Standard for ECG Connectors (AAMI ECGC-5/83)

American Society for Testing and Materials:

> Standard Practice for Performance Testing of Shipping Containers and Systems (D 4169)
>
> Standard Test Methods for Radiopacity of Plastics for Medical Use (F 640)

Military Standard Test Methods for Electronic and Electrical Component Parts (MIL-STD-202F, 1 April 1980). Five cycles of: 30 minutes at -55° +0/-3° C; 5 minutes at 25° +10/-5° C; 30 minutes at 85° +3/-0° C; and 5 minutes at 25° +10/-5° C.

DRAFT VERSION 0.98

March 14, 1995

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT*
(As Required By 21 CFR 807.87(j))

I certify that, in my capacity as [*The Position Held In Company*] of [*Company Name*], I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

[*Signature*]

____
[*Typed Name*]

____
[*Dated*]

____
[*Premarket Notification (510(k)) Number*]

* Must be signed by a responsible person of the firm required to submit the premarket notification (e.g., not a consultant for the 510(k) submitter.)

DRAFT VERSION 0.98

March 14, 1995

PREMARKET NOTIFICATION
510(k) STATEMENT
(As Required By 21 CFR 807.93)

I certify that, in my capacity as [*The Position Held In Company By Person Required To Submit The Premarket Notification, Preferably The Official Correspondent In The Firm*], of [*Company Name*], I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification submission is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential commercial information, as defined in 21 CFR 20.61.

[*Signature*]

____

[*Typed Name*]

____

[*Dated*]

____

[*Premarket Notification (510(k)) Number*]

ELECTRODE RECORDING CATHETER CHECKLIST

	Y	N	O
Intended Use	☐	☐	☐
Labeling			
Package Label	☐	☐	☐
Directions For Use	☐	☐	☐
Promotional Material	☐	☐	☐
Device Description			
Materials Specification	☐	☐	☐
Catheter Drawings	☐	☐	☐
Model Identification	☐	☐	☐
Accessory Cables	☐	☐	☐
Biocompatibility			
Sample Preparation	☐	☐	☐
Test Reports	☐	☐	☐
Sterility			
Routine Testing	☐	☐	☐
Sterility Test	☐	☐	☐
Sterilization Method	☐	☐	☐
Sterility Assurance Level	☐	☐	☐
Validation Method	☐	☐	☐
Packaging Description	☐	☐	☐
Packaging Validation	☐	☐	☐
Resterilization	☐	☐	☐
Performance Testing			
Reliability			
Thermal Cycling	☐	☐	☐
Tensile Testing	☐	☐	☐
Torsional Testing	☐	☐	☐
Joint Seal	☐	☐	☐
Leakage Current	☐	☐	☐
Deflection Fatigue	☐	☐	☐
Flexion Fatigue	☐	☐	☐
Connector	☐	☐	☐
Accessory Cable	☐	☐	☐
Open Lumen Catheters:			
Stylet Forces	☐	☐	☐
Infusion	☐	☐	☐
Leak	☐	☐	☐
Response	☐	☐	☐
Materials and Mechanical			
Torsion	☐	☐	☐
Deflection	☐	☐	☐
Steering	☐	☐	☐
Bending	☐	☐	☐
Buckling Force	☐	☐	☐
Radiopacity	☐	☐	☐
Electrical			
Impedance	☐	☐	☐
Noise	☐	☐	☐
Stimulation	☐	☐	☐
Mapping	☐	☐	☐
Quality Assurance	☐	☐	☐
510(k) Summary	☐		
510(k) Statement	☐		

Y: Yes or Complete
N: No or Incomplete
O: Omission Justified or Not Applicable

NOTES:______________________________
____
____